

AMENDMENTS TO THE SPECIFICATION

Please amend the specification as follows:

Please replace the paragraph appearing at page 16, lines 6-14 with the following amended paragraph:

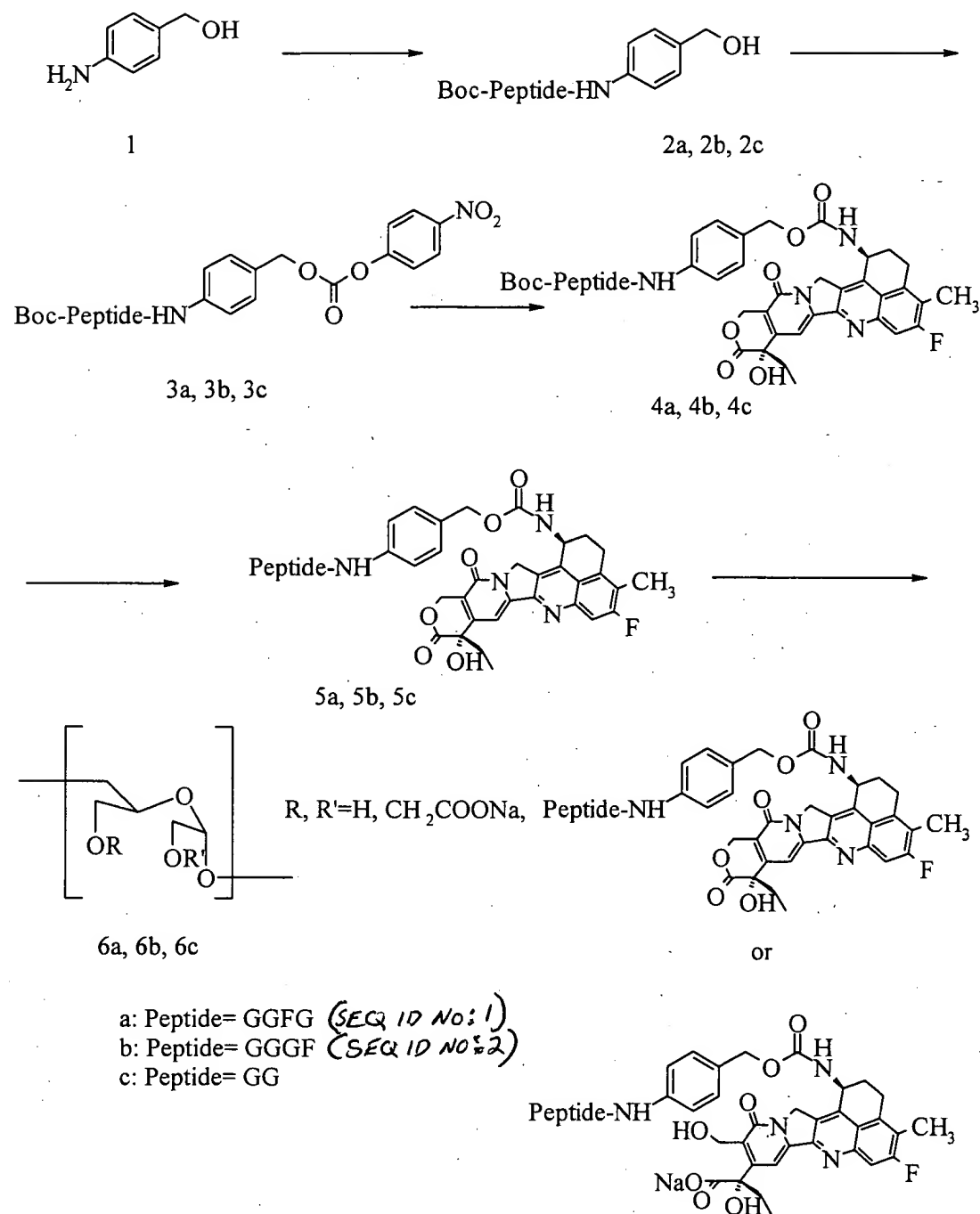
A compound of the present invention provided from another aspect is represented by the following general formula (II): $R'-NH-Y-CH_2-O-CO-Q$, wherein R' is a group comprising one amino acid or peptide-bonded 2 to 8 amino acids of which the N-terminal is protected or not protected; Y is phenylene group which may be substituted; and Q is a residue of a drug compound. In this compound, preferred are those wherein Y is unsubstituted p-phenylene group, R' is a group represented by H-Gly-Gly-Phe-Gly- (SEQ ID NO: 1) or H-Gly-Gly-Gly-Phe- (SEQ ID NO: 2), and the drug compound is (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-(9H,15H)-dione.

Please replace the paragraph appearing at page 17, lines 21 to page 18, line 4 with the following amended paragraph:

DX-8951 represents a drug compound: (1S,9S)-1-amino-9-ethyl-5-fluoro-2,3-dihydro-9-hydroxy-4-methyl-1H,12H-benzo[de]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-10,13-(9H,15H)-dione which was disclosed in claim 2 of Japanese Patent Unexamined Publication (KOKAI) (Hei) No. 6-87746/1994, and -CO-DX-8951 represents that the amino group at the 1-position of the drug compound forms a peptide bond with the carbonyl group represented by -CO-. It should be understood that DX-8951 has a lactone ring which exists in the ring-closed or ring-opened form, or in the form of the mixture thereof. The building units of the saccharide

chain shown in the following schemes are introduced with one or two carboxymethyl groups. It should be noted that this building units are shown as an example of the building unit of the saccharide chain, and that the drug carrier moiety of the drug complex of the present invention is not formed by the repetition of the above building unit. The compound numbers in the examples correspond to those in the following schemes. For example, Compound 2a in Example 5 corresponds to Compound 2a in the scheme, which represents a compound in which the peptide moiety of the formula in the scheme is GGFG (SEQ ID NO: 1) (In the scheme, this is shown as Peptide = GGFG.).

Please replace page 20 with the following amended page 20:



Example 1: Synthesis of carboxymethyl dextran polyalcohol-Gly-Gly-Phe-Gly-NH-p-C₆H₄-CH₂-O-CO-DX-8951 (SEQ ID NO: 1)

Dextran T500 (20 g, Pharmacia, molecular weight: 500K) was dissolved in 0.1 M acetic buffer (pH 5.5, 2,000 ml), and added with an aqueous solution (2,000 ml) of sodium periodate (66.0 g). The mixture was stirred at 4°C for 10 days with shielding

Please replace the paragraph appearing at page 21, lines 21-31 with the following amended paragraph:

1-Ethoxycarbonyl-2-ethoxy-1,2-dihydroxyquinoline (989 mg) was added to a mixture of Boc-Gly-Gly-Phe-Gly-OH (SEQ ID NO: 1) (875 mg), 4-aminobenzyl alcohol (492 mg) and N,N-dimethylformamide (10 ml). The resulting mixture was allowed to react with stirring at room temperature overnight, and then the reaction mixture was evaporated to dryness under reduced pressure. The residue was purified by silica gel column chromatography (eluate: a solution of dichloromethane:methanol = 96:4) to obtain 800 mg of Compound (2).

¹H-NMR (DMSO-d₆)δ: 9.73 (s, 1H), 8.38 (s, 1H), 8.17 (d, 1H, J=7.2Hz), 7.91-7.93 (m, 1H), 7.56 (d, 2H, J=8.0Hz), 7.24-7.26 (m, 4H), 7.24 (d, 2H, J=8.0Hz), 7.17-7.20 (m, 1H), 4.50-4.54 (m, 1H), 4.44 (s, 2H), 3.66-3.94 (m, 3H), 3.63 (dd, 1H, J=4.8,16.7Hz), 3.56 (d, 2H, J=5.6Hz), 3.09 (dd, 1H, J=4.8,13.5Hz), 2.83 (dd, 1H, J=9.6,13.5Hz), 1.38 (s, 9H).

Please replace the paragraph appearing at page 26, lines 1 and 2 (following the Table) with the following amended paragraph:

Example 5: Synthesis of carboxymethyldextran polyalcohol-Gly-Gly-Phe-Gly-NH-p-C₆H₄-CH₂-O-CO-DX-8951 (SEQ ID NO: 1) using formic acid as a deprotecting agent

Please replace the paragraph appearing at page 27, lines 7-17 with the following amended paragraph:

1-Ethoxycarbonyl-2-ethoxy-1,2-dihydroxyquinoline (989 mg) was added to a mixture of Boc-Gly-Gly-Phe-Gly-OH (SEQ ID NO: 1) (875 mg), 4-aminobenzyl alcohol (492 mg) and N,N-dimethylformamide (10 ml). The resulting mixture was allowed to react with stirring at room temperature overnight, and then the reaction mixture was evaporated to dryness under reduced pressure. The residue was purified by silica gel column chromatography (eluate: a solution of dichloromethane:methanol = 96:4) to obtain 800 mg of Compound 2a.

¹H-NMR (DMSO-d₆)δ: 9.73 (s, 1H), 8.38 (s, 1H), 8.17 (d, 1H, J=7.2Hz), 7.91-7.93 (m, 1H), 7.56 (d, 2H, J=8.0Hz), 7.24-7.26 (m, 4H), 7.24 (d, 2H, J=8.0Hz), 7.17-7.20 (m, 1H), 4.50-4.54 (m, 1H), 4.44 (s, 2H), 3.66-3.94 (m, 3H), 3.63 (dd, 1H, J=4.8,16.7Hz), 3.56 (d, 2H, J=5.6Hz), 3.09 (dd, 1H, J=4.8,13.5Hz), 2.83 (dd, 1H, J=9.6,13.5Hz), 1.38 (s, 9H).

Please replace the paragraph appearing at page 29, lines 21 and 22 with the following amended paragraph:

Example 6: Synthesis of carboxymethyldextran polyalcohol-Gly-Gly-Gly-Phe-NH-p-C₆H₄-CH₂-O-CO-DX-8951 (SEQ ID NO: 2) using formic acid as a deprotecting agent

Please replace the paragraph appearing at page 30, lines 15 to 26 with the following amended paragraph:

1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide (571 mg) was added to a mixture of Boc-Gly-Gly-Gly-Phe-OH SEQ ID NO: 2 (1,000 mg), 4-aminobenzyl alcohol (324 mg), 1-hydroxybenzotriazole (464 mg) and N,N-dimethylformamide (10 ml). The resulting mixture was allowed to react with stirring at room temperature overnight, and then the reaction mixture was evaporated to dryness under reduced pressure. The residue was purified by silica gel column chromatography (eluate: a solution of dichloromethane:methanol = 92:8) to obtain Compound 2b (1,220 mg).

¹H-NMR (DMSO-d₆)δ: 9.91 (s, 1H), 8.25 (d, 1H, J=3.7Hz), 8.08-8.20 (m, 2H), 7.54 (d, 2H, J=8.3Hz), 7.25-7.29 (m, 4H), 7.23 (d, 2H, J=8.3Hz), 7.16-7.21 (m, 1H), 6.95 (t, 1H, J=5.9Hz), 5.08 (d, 1H, J=5.9Hz), 4.62-4.67 (m, 1H), 4.44 (d, 2H, J=5.9Hz), 3.74 (dd, 1H, J=4.9, 5.4Hz), 3.65 (dd, 1H, J=5.9, 16.6Hz), 3.59 (d, 2H, J=5.4Hz), 3.07 (dd, 1H, J=5.4, 13.7Hz), 2.90 (dd, 1H, J=9.3, 13.7Hz), 1.37 (s, 9H).

IN THE TILE

Please change the Title of the Invention to:

DRUG COMPLEX AND DRUG DELIVERY SYSTEM